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QSPR models for polychlorinated biphenyls: *n*-Octanol/water partition coefficient

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Abstract—The logarithmic *n*-octanol/water partition coefficient ($\log K_{ow}$) is an important property for pharmacology, toxicology and medicinal chemistry. Quantitative structure–property relationship (QSPR) model for the lipophilic behaviour ($\log K_{ow}$) of the data set containing 133 polychlorinated biphenyl (PCB) congeners is analyzed using the conceptual density functional theory based global reactivity parameter such as electrophilicity index (ω) along with energy of lowest unoccupied molecular orbital (E_{LUMO}) and number of chlorine substituents (N_{Cl}) as descriptors. A reasonably good coefficient of determination ($r^2 = 0.914$) and the internal predictive ability ($r^2_{cv} = 0.909$) values are obtained indicating the significance of the considered descriptors in the property analysis of PCBs. Further, the developed method has widespread applicability from chemical reactivity to toxicity analysis and in studies related to various physicochemical properties in the series of dioxins and other polyaromatic hydrocarbons.

1. Introduction

Polychlorinated biphenyls are persistent organic contaminants and widespread environmental pollutants that are found at an appreciable concentration in the polar regions presumably as a result of long-range atmospheric transport.[1] Toxicological effects of exposure to polychlorinated biphenyl (PCBs) include hepatotoxicity, immunotoxicity and reproductive problems, as well as respiratory, mutagenic and carcinogenic effects.[2,3] Structure–activity relationship studies trace out the fact that PCB-induced body weight loss, thymic atrophy and carcinogenicity are associated with high affinity for aryl hydrocarbon (Ah) receptor.[4] The non-inflammability and chemical stability associated with the PCBs has contributed to the widespread environmental problems. It is possible to observe from the toxicity data that there are only 12 PCBs, which have been identified as toxic, out of 209 PCB congeners. These compounds exhibit toxicity similar to that of polychlorinated dibenzo-*p*-dioxin (PCDD). All this information on PCBs has prompted several investigators to understand the toxic nature of PCBs and their interaction with cellular components.[5] The origin of toxicity of PCDDs has been attributed to the electron-accepting nature in charge transfer complex with a receptor in living cells. The oxidative DNA damage induced by PCBs and their implication in breast cancer has been addressed.[4] Hence, electron affinity of PCBs is used as an important quantity in understanding their toxic effects. Accordingly, the calculation of electron affinity of various PCBs has attracted recent theoretical interests.

There have been many reports on the prediction of $\log K_{ow}$ for PCBs, because the compounds have serious ecologically harmful effects and are implicated as potent carcinogens.[6] Most of the reported prediction methods are based on (i) a substituent constant approach,[7] (ii) thermodynamically oriented theories.[8,9] In addition to this, (iii) connectivity indexes[10–14] and characteristic root index (CRI)[15] of the biphenyl skeleton of PCBs have also been reported as useful descriptors to predict the $\log K_{ow}$. Those descriptors are based on topological properties of PCBs, and it has been elucidated that the values are very closely related to the molecular volume and/or the total surface area.[16] It has been reported, moreover, that (iv) molecular refraction is also an important descriptor to predict the $\log K_{ow}$.[17] On the other hand, it is true that ionization potential (I), electronic affinity (EA), and dipole moment (p), which are

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calculated on the basis of quantum chemistry, are also significant physicochemical properties of PCB molecules. It is expected that these properties may explain the new partition behaviour of PCBs since the above descriptors (connectivity indexes, etc.) are not directly including the molecular characteristics based on the quantum chemistry. Further, it has been reported that there is a strong relationship between gas chromatographic retention indices and those parameters (I, EA and p).[18]

Three-dimensional structure–property correlations for prediction of thermodynamic properties of PCBs have been recently made to predict the enthalpy of vapourization and enthalpy of sublimation.[19,20] The octanol/water partition coefficient expressed as $\log K_{ow}$ is an important property for various applications in pharmacology, toxicology and medicinal chemistry.[21] $\log K_{ow}$ is used to model partitioning of chemicals between the lipophilic membrane and the relative hydrophobic cellular cytoplasmic material. $\log K_{ow}$ quantifies hydrophobicity of chemicals and is important both for predicting pharmacokinetics and pharmacodynamics of drugs and toxicants.[22] Lipophilicity is traditionally measured in the octanol/water system. $\log K_{ow}$ values have been shown to be generally satisfactory for modelling protein binding and lipophilic interactions with biological membranes consisting largely of protein.[23] Several methods have been described in the literature for the estimation of the octanol/water partition coefficient, which is $\log K_{ow}$.[24,25]

Conceptual density functional theory has been successfully exploited to unravel chemical reactivity and site selectivity.[26,27] Recently, our group has carried out toxicity analysis on PCBs and other systems using density functional theory (DFT) based descriptors.[28–31] In the present study, we have analyzed the quantitative structure–property relationship (QSPR) for $\log K_{ow}$ of the selected 133 PCB congeners based on electrophilicity (ω), accompanied with lowest unoccupied molecular orbital (E_{LUMO}) energy and number of chlorine substituents (N_{Cl}) as descriptors.

2. Theoretical background

According to the density functional theory,[32,33] the chemical potential (μ) and chemical hardness (η) are defined as

$$\chi = -\mu = -\left(\frac{\partial E}{\partial N}\right)_{v(\vec{r})} \tag{1}$$

and

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right)_{v(\vec{r})} = \frac{1}{2}\left(\frac{\partial \mu}{\partial N}\right)_{v(\vec{r})}, \tag{2}$$

where E is the total energy of the system, N is the number of electrons in the system and $v(\vec{r})$ is the external potential. μ is identified as the negative of the electronegativity (χ) as defined by Iczkowski and Margrave.[34]

The vertical ionization potential (IP) of a system is the change of energy when an electron is removed from the system and variation of the energy when an electron is added to the system, known as electron affinity (EA). In both the cases of electron withdrawing and electron addition, the external potential has to be kept fixed. Hence, using finite difference approximation, Eqs. 1 and 2 become

$$\mu = -\frac{(\mathrm{IP} + \mathrm{EA})}{2} \tag{3}$$

$$\eta = \frac{\mathrm{IP} - \mathrm{EA}}{2}. \tag{4}$$

However, to obtain the IP and EA and hence μ and η, one needs three energy values (E_N, E_{N+1} and E_{N-1}). To save computational time, we have calculated chemical potential and chemical hardness by using Koopmans' theorem[33] as

$$\mu = \frac{E_{LUMO} + E_{HOMO}}{2} \tag{5}$$

and

$$\eta = \frac{E_{LUMO} - E_{HOMO}}{2}, \tag{6}$$

where E_{LUMO} is the lowest unoccupied molecular orbital's energy and E_{HOMO} is the highest occupied molecular orbital's energy.

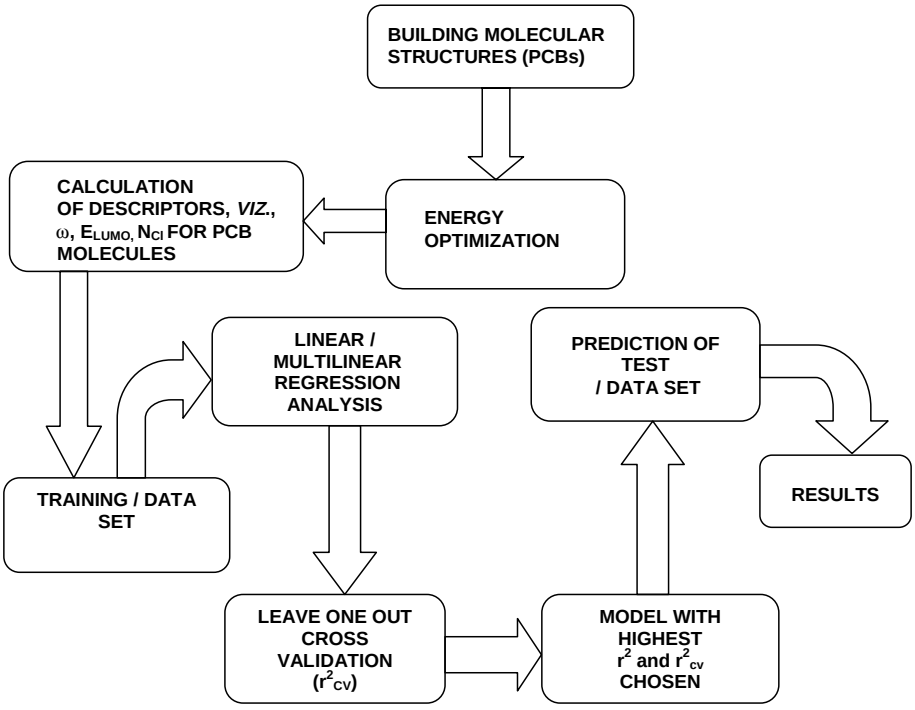
Parr et al.[35] introduced the global electrophilicity index (ω) in terms of chemical potential and hardness as

$$\omega = \frac{\mu^2}{2\eta}. \tag{7}$$

3. Method for data analysis

The set of 133 PCB congeners considered in this study is divided into two groups, namely, the training set and the test set. Test set consists of 25% (33 congeners) of the entire set of 133 PCB congeners, which includes at least one PCB congener from various chlorine substituent levels and the training set contains the remaining 100 PCB congeners. Initially, linear/multilinear regression analyses are performed using experimental $\log K_{ow}$ as dependent variable and various combinations of the selected descriptors as independent variables on the training set. Internal validations of the model for the training set have been performed using cross-validation.[36,37] In cross-validation, a model is calculated with groups of object (PCB congeners) omitted subsequently, followed by the prediction of the target property for the omitted objects. In the present study, Leave-one-out (LOO) method is adopted and the procedure is repeated until all the objects have been omitted once. Internal predictability of the models is characterized by the cross-validated squared correlation coefficient (r^2_{cv}) given by

$$r^2_{cv} = 1 - \frac{\sum_i (Y_i^{pred} - Y_i^{obs})^2}{\sum_i (Y_i^{obs} - Y^{mean})^2}, \tag{8}$$



Scheme 1. The process of QSPR modelling with cross-validation for the selected set of polychlorinated biphenyls.

where Y_i^{obs}, Y_i^{pred} and Y^{mean} are, respectively, the observed, predicted, and observed mean values of the dependent variables; the summations run over all compounds in the training set.

The resulting best model using the training set has been chosen to predict the $\log K_{ow}$ values of the PCBs in the test set. Then, the training and test sets are combined and the above process of regression analysis and validation is carried out on this data set to select the best model for prediction. Scheme 1 elaborates the above-mentioned process in a lucid and elegant manner.

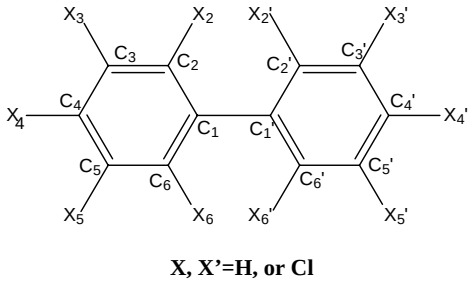


Figure 1. Geometry of biphenyl template with atom numbering.

4. Computational details

The geometry of biphenyl template is depicted along with atom numbering (Fig. 1). The geometries of 133 PCB congeners are optimized using semi-empirical AM1 method as implemented in the Gaussian 03 package[38] and the values of global electrophilicity index (ω) are calculated using Eq. 7. One-, two- and three-parameter QSAR[39] are performed using least square error estimation method[40] to calculate the $\log K_{ow}$ values.

5. Results and discussion

Regression models for the training set of 100 PCB congeners with experimental $\log K_{ow}$ values[12,41] taken as dependent variables and all possible combinations of the three descriptors, such as the electrophilicity index (ω) with lowest unoccupied molecular orbital (E_{LUMO}) energy and number of chlorine substituents (N_{Cl}) as independent variables, are presented in Table 1. It has

Table 1. Regression models for $\log K_{ow}$ using various descriptors for training set of 100 PCB congeners

S.No.	Regression equation	r^2	r^2_{cv}	SD
1	$\log K_{ow} = 4.686–72.141*E_{LUMO}$	0.774	0.765	0.320
2	$\log K_{ow} = 4.335 + 0.395*N_{Cl}$	0.832	0.826	0.276
3	$\log K_{ow} = -2.141 + 78.870*\omega$	0.861	0.855	0.251
4	$\log K_{ow} = 4.299 + 0.252*N_{Cl} - 33.336*E_{LUMO}$	0.888	0.881	0.227
5	$\log K_{ow} = -9.836 + 88.670*E_{LUMO} + 169.340*\omega$	0.897	0.890	0.217
6	$\log K_{ow} = 0.346 + 0.186*N_{Cl} + 46.958*\omega$	0.905	0.899	0.209
7	$\log K_{ow} = -4.827 + 0.135*N_{Cl} + 51.701*E_{LUMO} + 108.513*\omega$	0.914	0.906	0.199

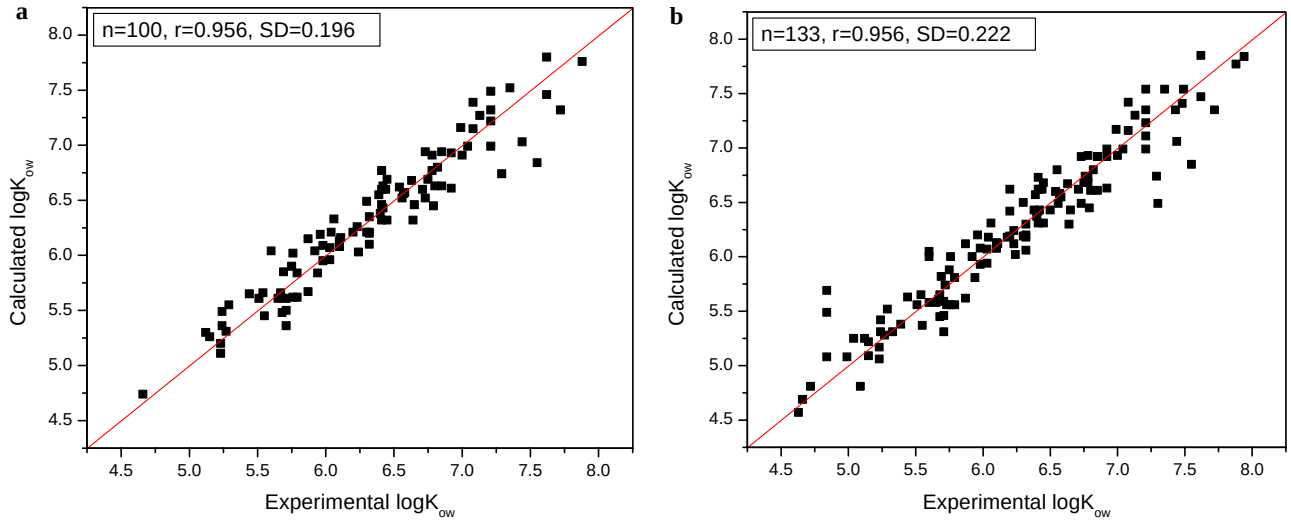


Figure 2. Experimental versus calculated values of log K_{ow} with electrophilicity, E_{LUMO} and N_{Cl} as descriptors for the model constructed using (a) the training set of 100 PCBs; (b) the data set of 133 PCBs.

Table 2. Experimental and calculated values of log K_{ow} for the model test set with the model constructed using the training set

IUPAC No.	Compounds	Descriptors			Log K_{ow}[a] values		
		ω	E_{LUMO}	N_{Cl}	Exp.[b]	Calculated	Residual[c]
3	4-Chlorobiphenyl	0.085	0.002	1	4.63	4.57	0.06
4	2,2′-Dichlorobiphenyl	0.086	0.002	2	4.72	4.77	−0.05
5	2,3-Dichlorobiphenyl	0.094	−0.01	2	4.99	5.00	−0.01
6	2,3′-Dichlorobiphenyl	0.094	−0.01	2	4.84	5.00	−0.16
7	2,4-Dichlorobiphenyl	0.096	−0.014	2	5.15	4.91	0.24
8	2,4′-Dichlorobiphenyl	0.087	0.000	2	5.09	4.72	0.37
17	2,2′,4-Trichlorobiphenyl	0.095	−0.009	3	5.39	5.35	0.04
18	2,2′,5-Trichlorobiphenyl	0.094	−0.008	3	5.33	5.25	0.08
19	2,2′,6-Trichlorobiphenyl	0.092	−0.005	3	5.04	5.19	−0.15
20	2,3,3′-Trichlorobiphenyl	0.100	−0.016	3	5.60	5.57	0.03
21	2,3,4-Trichlorobiphenyl	0.102	−0.019	3	5.68	5.63	0.05
42	2,2′,3,4′-Tetrachlorobiphenyl	0.099	−0.013	4	5.72	5.71	0.01
44	2,2′,3,5′-Tetrachlorobiphenyl	0.097	−0.012	4	5.73	5.36	0.37
45	2,2′,3,6-Tetrachlorobiphenyl	0.100	−0.016	4	4.84	5.52	−0.68
46	2,2′,3,6′-Tetrachlorobiphenyl	0.095	−0.009	4	4.84	5.30	−0.46
85	2,2′,3,4,4′-Pentachlorobiphenyl	0.105	−0.02	5	6.18	6.13	0.05
86	2,2′,3,4,5-Pentachlorobiphenyl	0.109	−0.024	5	6.38	6.55	−0.17
87	2,2′,3,4,5′-Pentachlorobiphenyl	0.104	−0.019	5	6.23	6.03	0.20
88	2,2′,3,4,6-Pentachlorobiphenyl	0.109	−0.024	5	6.50	6.55	−0.05
89	2,2′,3,4,6′-Pentachlorobiphenyl	0.102	−0.016	5	5.60	5.97	−0.37
129	2,2′,3,3′,4,5-Hexachlorobiphenyl	0.112	−0.027	6	6.76	6.80	−0.04
130	2,2′,3,3′,4,5′-Hexachlorobiphenyl	0.108	−0.023	6	7.30	6.39	0.91
131	2,2′,3,3′,4,6-Hexachlorobiphenyl	0.112	−0.028	6	6.78	6.66	0.12
132	2,2′,3,3′,4,6′-Hexachlorobiphenyl	0.107	−0.022	6	6.20	6.29	−0.09
134	2,2′,3,3′,5,6-Hexachlorobiphenyl	0.111	−0.027	6	6.20	6.55	−0.35
172	2,2′,3,3′,4,5,5′-Heptachlorobiphenyl	0.116	−0.031	7	7.21	7.17	0.04
174	2,2′,3,3′,4,5,6′-Heptachlorobiphenyl	0.113	−0.028	7	6.85	6.86	−0.01
175	2,2′,3,3′,4,5′,6-Heptachlorobiphenyl	0.115	−0.031	7	6.92	6.92	0.00
176	2,2′,3,3′,4,6,6′-Heptachlorobiphenyl	0.112	−0.028	7	6.55	6.61	−0.06
196	2,2′,3,3′,4,4′,5,6′-Octachlorobiphenyl	0.118	−0.033	8	7.43	7.32	0.11
203	2,2′,3,4,4′,5,5′,6-Octachlorobiphenyl	0.121	−0.036	8	7.49	7.63	−0.14
204	2,2′,3,4,4′,5,6,6′-Octachlorobiphenyl	0.119	−0.034	8	7.48	7.43	0.05
206	2,2′,3,3′,4,4′,5,5′,6-Nonachlorobiphenyl	0.124	−0.039	9	7.94	7.89	0.05

[a] With ω (in au), E_{LUMO} (in au) and N_{Cl} as descriptors.
[b] Experimental data as obtained from Refs. 12 and 41.
[c] The residual is the difference between experimental and predicted log K_{ow} values.

Table 3. Regression models for $\log K_{ow}$ using various descriptors for a data set of 133 PCB congeners

S.No.	Regression equation	r^2	r^2_{cv}	SD
1	$\log K_{ow} = 4.617–75.219*E_{LUMO}$	0.811	0.806	0.330
2	$\log K_{ow} = 4.234 + 0.406*N_{Cl}$	0.842	0.838	0.302
3	$\log K_{ow} = -2.446 + 81.693*\omega$	0.877	0.874	0.266
4	$\log K_{ow} = 4.262 + 0.243*N_{Cl} - 36.119*E_{LUMO}$	0.892	0.888	0.251
5	$\log K_{ow} = -10.523 + 91.620*E_{LUMO} + 176.280*\omega$	0.905	0.901	0.235
6	$\log K_{ow} = -0.038 + 0.173*N_{Cl} + 51.015*\omega$	0.906	0.902	0.234
7	$\log K_{ow} = -5.967 + 0.115*N_{Cl} + 58.070*E_{LUMO} + 121.280*\omega$	0.914	0.909	0.225

been inferred from Table 1 that the regression model developed using all the three descriptors as independent variables is capable of explaining maximum variation in data ($r^2 = 91.4\%$) with leave-one-out cross-validated squared correlation coefficient ($r^2_{cv} = 0.906$) and a low value for root mean square deviation (SD = 0.199). A plot between the experimental and the calculated $\log K_{ow}$ values gives a good correlation coefficient (r) of 0.956 (Fig. 2a). The developed three-parameter regression model is used to predict the $\log K_{ow}$ values of the PCB congeners in the test set (Table 2). The low residual values obtained between the experimental and the calculated $\log K_{ow}$ values reveal the importance of the selected descriptors in QSPR analysis on PCBs.

5.1. Analysis on the combined set of PCBs

Initially, direct correlation analyses are carried out between the calculated descriptors and experimental $\log K_{ow}$ values. The electrophilicity index (ω) along with lowest unoccupied molecular orbital (E_{LUMO}) energy and number of chlorine substituents (N_{Cl}) are used to develop one, two and three parameter models for structure property analysis, for which the experimental $\log K_{ow}$ values of the combined set (training and test sets) acted as dependent variables. The regression equations along with coefficient of determination (r^2), LOO cross-validated squared correlation coefficient (r^2_{cv}) and root mean square deviation (SD) for several combinations of the descriptors for the complete data set of 133 PCB congeners are given in Table 3.

5.2. Linear regression with descriptors

Correlations have been made between the calculated individual descriptors and the experimental $\log K_{ow}$ values. Table 3 describes that, among the three descriptors selected, electrophilicity index (ω) is capable of providing maximum variation in data ($r^2 = 87.7\%$) compared to the other two descriptors. There is an average increase in the value of electrophilicity index (ω) with increase in the experimental $\log K_{ow}$ values. It is also interesting to note that the lower the E_{LUMO} value, the greater are the intermolecular interactions between octanol and PCB molecules and the greater are the $\log K_{ow}$ values. Also, with an increase in the value of chlorine atom substitution (N_{Cl}), there is an increase in the value of $\log K_{ow}$. Thus, all the three descriptors selected in the present study seem to be uniquely linked with the experimental $\log K_{ow}$ values of PCB congeners.

5.3. Multilinear regression with descriptors

Activities of molecules in the biological system are highly influenced by their inherent electronic properties as well as size. Hence, electrophilicity index (ω) along with E_{LUMO} and N_{Cl} are considered as useful descriptors in analyzing the transportability property that is, $\log K_{ow}$. Among the two-descriptor combination, electrophilicity index (ω) along with a number of chlorine substituents provides maximum coefficient of determination ($r^2 = 0.906$). Using all three descriptors in the QSPR model, for the combined set of 133 PCB congeners, we get maximum values for the coefficient of determination ($r^2 = 0.914$) and cross-validated squared correlation coefficient ($r^2_{cv} = 0.909$) (Table 3). Table 4 lists the experimental and the calculated $\log K_{ow}$ values for the selected set of 133 PCB congeners obtained using all three selected descriptors. A plot between the experimental and the calculated $\log K_{ow}$ values gives a correlation coefficient (r) of 0.956 (Fig. 2b). This evidently reveals the fact that the electrophilicity index (ω) along with lowest unoccupied molecular orbital (E_{LUMO}) energy and number of chlorine substituents (N_{Cl}) can be effectively used as descriptors in QSPR analysis on PCBs. The descriptors used and the method adopted in this study can be easily extended for application in QSPR studies on dioxins and other polyaromatic hydrocarbon related systems.

6. Conclusions

The success of any QSPR model depends on the selection of appropriate descriptors. Exploring the usefulness of descriptors, especially, conceptual DFT based descriptors along with other descriptors and analyzing their applicability could lead to drastic improvement in QSPR models. Based on this fact, structure–property relationship for the data set containing 133 polychlorinated biphenyl (PCB) congeners on the lipophilic behaviour ($\log K_{ow}$) is analyzed. Traditional regression procedures along with cross-validation are carried out to evaluate the predicting power of the developed model. It has been shown that using the entire data set, the global electrophilicity index (ω) with E_{LUMO} and a number of chlorine substituents as descriptors provides a reasonably good coefficient of determination

Table 4. Experimental and calculated values of $\log K_{ow}$ for the model constructed using the data set of 133 PCB congeners

IUPAC No.	Compounds	Descriptors			$\log K_{ow}$[a] values		
		ω	E_{LUMO}	N_{Cl}	Exp.[b]	Calculated	Residual[c]
2	3-Chlorobiphenyl	0.085	0.004	1	4.66	4.69	−0.03
3	4-Chlorobiphenyl	0.085	0.002	1	4.63	4.57	0.06
4	2,2′-Dichlorobiphenyl	0.086	0.002	2	4.72	4.81	−0.09
5	2,3-Dichlorobiphenyl	0.094	−0.010	2	4.99	5.08	−0.09
6	2,3′-Dichlorobiphenyl	0.094	−0.010	2	4.84	5.08	−0.24
7	2,4-Dichlorobiphenyl	0.096	−0.014	2	5.15	5.09	0.06
8	2,4′-Dichlorobiphenyl	0.087	0.000	2	5.09	4.81	0.28
11	3,3′-Dichlorobiphenyl	0.099	−0.017	2	5.27	5.28	−0.01
12	3,4-Dichlorobiphenyl	0.099	−0.019	2	5.23	5.17	0.06
13	3,4′-Dichlorobiphenyl	0.099	−0.018	2	5.15	5.22	−0.07
15	4,4′-Dichlorobiphenyl	0.09	−0.002	2	5.23	5.06	0.17
16	2,2′,3-Trichlorobiphenyl	0.092	−0.005	3	5.12	5.25	−0.13
17	2,2′,4-Trichlorobiphenyl	0.095	−0.009	3	5.39	5.38	0.01
18	2,2′,5-Trichlorobiphenyl	0.094	−0.008	3	5.33	5.31	0.02
19	2,2′,6-Trichlorobiphenyl	0.092	−0.005	3	5.04	5.25	−0.21
20	2,3,3′-Trichlorobiphenyl	0.100	−0.016	3	5.60	5.58	0.02
21	2,3,4-Trichlorobiphenyl	0.102	−0.019	3	5.68	5.65	0.03
22	2,3,4′-Trichlorobiphenyl	0.100	−0.017	3	5.29	5.52	−0.23
24	2,3,6-Trichlorobiphenyl	0.100	−0.015	3	5.44	5.63	−0.19
25	2,3′,4-Trichlorobiphenyl	0.102	−0.019	3	5.54	5.65	−0.11
26	2,3′,5-Trichlorobiphenyl	0.101	−0.018	3	5.65	5.58	0.07
28	2,4,4′-Trichlorobiphenyl	0.102	−0.020	3	5.71	5.59	0.12
31	2,4′,5-Trichlorobiphenyl	0.097	−0.012	3	5.68	5.45	0.23
32	2,4′,6-Trichlorobiphenyl	0.094	−0.008	3	5.24	5.31	−0.07
33	2,3′,4′-Trichlorobiphenyl	0.100	−0.018	3	5.71	5.46	0.25
34	2,3′,5′-Trichlorobiphenyl	0.093	−0.006	3	5.71	5.31	0.40
40	2,2′,3,3′-Tetrachlorobiphenyl	0.096	−0.009	4	5.67	5.61	0.06
41	2,2′,3,4-Tetrachlorobiphenyl	0.101	−0.016	4	5.79	5.81	−0.02
42	2,2′,3,4′-Tetrachlorobiphenyl	0.099	−0.013	4	5.72	5.74	−0.02
44	2,2′,3,5′-Ttetrachlorobiphenyl	0.097	−0.012	4	5.73	5.56	0.17
45	2,2′,3,6-Tetrachlorobiphenyl	0.100	−0.016	4	4.84	5.69	−0.85
46	2,2′,3,6′-Tetrachlorobiphenyl	0.095	−0.009	4	4.84	5.49	−0.65
47	2,2′,4,4′-Tetrachlorobiphenyl	0.100	−0.014	4	5.94	5.81	0.13
48	2,2′,4,5-Tetrachlorobiphenyl	0.102	−0.018	4	5.69	5.82	−0.13
49	2,2′,4,5′-Tetrachlorobiphenyl	0.098	−0.013	4	5.87	5.62	0.25
50	2,2′,4,6-Tetrachlorobiphenyl	0.102	−0.017	4	5.75	5.88	−0.13
51	2,2′,4,6′-Tetrachlorobiphenyl	0.096	−0.010	4	5.51	5.56	−0.05
52	2,2′,5,5′-Tetrachlorobiphenyl	0.097	−0.012	4	5.79	5.56	0.23
53	2,2′,5,6′-Tetrachlorobiphenyl	0.094	−0.009	4	5.55	5.37	0.18
54	2,2′,6,6′-Tetrachlorobiphenyl	0.093	−0.006	4	5.24	5.42	−0.18
55	2,3,3′,4-Tetrachlorobiphenyl	0.107	−0.024	4	6.10	6.08	0.02
60	2,3,4,4′-Tetrachlorobiphenyl	0.107	−0.025	4	6.24	6.02	0.22
63	2,3,4′,5-Ttetrachlorobiphenyl	0.107	−0.024	4	6.10	6.08	0.02
64	2,3,4′,6-Tetrachlorobiphenyl	0.104	−0.019	4	5.76	6.00	−0.24
65	2,3,5,6-Tetrachlorobiphenyl	0.108	−0.024	4	5.96	6.20	−0.24
66	2,3′,4,4′-Tetrachlorobiphenyl	0.108	−0.026	4	5.98	6.08	−0.10
67	2,3′,4,5-Tetrachlorobiphenyl	0.109	−0.026	4	6.32	6.20	0.12
69	2,3′,4,6-Tetrachlorobiphenyl	0.105	−0.02	4	6.03	6.07	−0.04
71	2,3′,4′,6-Tetrachlorobiphenyl	0.097	−0.012	4	5.76	5.56	0.2
74	2,4,4′,5-Tetrachlorobiphenyl	0.106	−0.021	4	6.10	6.13	−0.03
75	2,4,4′,6-Tetrachlorobiphenyl	0.104	−0.02	4	6.03	5.94	0.09
76	2,3′,4′,5′-Tetrachlorobiphenyl	0.102	−0.016	4	5.98	5.93	0.05
84	2,2′,3,3′,6-Pentachlorobiphenyl	0.103	−0.019	5	5.60	6.00	−0.4
85	2,2′,3,4,4′-Ppentachlorobiphenyl	0.105	−0.02	5	6.18	6.18	0.00
86	2,2′,3,4,5-Ppentachlorobiphenyl	0.109	−0.024	5	6.38	6.43	−0.05
87	2,2′,3,4,5′-Pentachlorobiphenyl	0.104	−0.019	5	6.23	6.12	0.11
88	2,2′,3,4,6-Pentachlorobiphenyl	0.109	−0.024	5	6.50	6.43	0.07
89	2,2′,3,4,6′-Pentachlorobiphenyl	0.102	−0.016	5	5.60	6.05	−0.45
90	2,2′,3,4′,5-Pentachlorobiphenyl	0.105	−0.020	5	6.32	6.18	0.14
91	2,2′,3,4′,6-Pentachlorobiphenyl	0.104	−0.019	5	5.87	6.12	−0.25
92	2,2′,3,5,5′-Pentachlorobiphenyl	0.104	−0.02	5	6.32	6.06	0.26
93	2,2′,3,5,6-Pentachlorobiphenyl	0.108	−0.024	5	6.06	6.31	−0.25
95	2,2′,3,5′,6-Pentachlorobiphenyl	0.103	−0.019	5	5.92	6.00	−0.08
97	2,2′,3,4′,5′-Pentachlorobiphenyl	0.106	−0.022	5	6.30	6.19	0.11
98	2,2′,3,4′,6′-Pentachlorobiphenyl	0.105	−0.02	5	6.04	6.18	−0.14

Table 4 (*continued*)

IUPAC No.	Compounds	Descriptors			Log K_{ow}[a] values		
		ω	E_{LUMO}	N_{Cl}	Exp.[b]	Calculated	Residual[c]
99	2,2′,4,4′,5-Pentachlorobiphenyl	0.107	−0.022	5	6.41	6.31	0.10
100	2,2′,4,4′,6-Pentachlorobiphenyl	0.106	−0.021	5	6.23	6.24	−0.01
103	2,2′,4,5′,6-Pentachlorobiphenyl	0.105	−0.021	5	6.11	6.12	−0.01
105	2,3,3′,4,4′-Pentachlorobiphenyl	0.112	−0.03	5	6.79	6.45	0.34
106	2,3,3′,4,5-Pentachlorobiphenyl	0.114	−0.031	5	6.92	6.63	0.29
110	2,3,3′,4′,6-Pentachlorobiphenyl	0.106	−0.022	5	6.2	6.19	0.01
112	2,3,3′,5,6-Pentachlorobiphenyl	0.112	−0.027	5	6.41	6.62	−0.21
113	2,3,3′,5′,6-Pentachlorobiphenyl	0.107	−0.022	5	6.45	6.31	0.14
114	2,3,4,4′,5-Pentachlorobiphenyl	0.112	−0.027	5	6.71	6.62	0.09
115	2,3,4,4′,6-Pentachlorobiphenyl	0.112	−0.027	5	6.44	6.62	−0.18
117	2,3,4′,5,6-Pentachlorobiphenyl	0.112	−0.028	5	6.39	6.57	−0.18
118	2,3′,4,4′,5-Pentachlorobiphenyl	0.114	−0.032	5	6.57	6.58	−0.01
119	2,3′,4,4′,6-Pentachlorobiphenyl	0.108	−0.023	5	6.40	6.37	0.03
120	2,3′,4,5,5′-Pentachlorobiphenyl	0.11	−0.025	5	6.30	6.50	−0.20
121	2,3′,4,5′,6-Pentachlorobiphenyl	0.109	−0.024	5	6.42	6.43	−0.01
123	2,3′,4,4′,5′-Pentachlorobiphenyl	0.106	−0.020	5	6.64	6.30	0.34
129	2,2′,3,3′,4,5-Hexachlorobiphenyl	0.112	−0.027	6	6.76	6.74	0.02
130	2,2′,3,3′,4,5′-Hexachlorobiphenyl	0.108	−0.023	6	7.30	6.49	0.81
131	2,2′,3,3′,4,6-Hexachlorobiphenyl	0.112	−0.028	6	6.78	6.68	0.10
132	2,2′,3,3′,4,6′-Hexachlorobiphenyl	0.107	−0.022	6	6.20	6.42	−0.22
134	2,2′,3,3′,5,6-Hexachlorobiphenyl	0.111	−0.027	6	6.20	6.62	−0.42
135	2,2′,3,3′,5,6′-Hexachlorobiphenyl	0.106	−0.022	6	6.32	6.30	0.02
137	2,2′,3,4,4′,5-Hexachlorobiphenyl	0.113	−0.028	6	6.82	6.80	0.02
138	2,2′,3,4,4′,5′-Hexachlorobiphenyl	0.109	−0.025	6	6.73	6.49	0.24
140	2,2′,3,4,4′,6′-Hexachlorobiphenyl	0.109	−0.024	6	6.58	6.55	0.03
141	2,2′,3,4,5,5′-Hexachlorobiphenyl	0.112	−0.028	6	6.75	6.68	0.07
143	2,2′,3,4,5,6′-Hexachlorobiphenyl	0.109	−0.025	6	6.56	6.49	0.07
144	2,2′,3,4,5′,6-Hexachlorobiphenyl	0.112	−0.028	6	6.45	6.68	−0.23
146	2,2′,3,4′,5,5′-Hexachlorobiphenyl	0.110	−0.025	6	6.85	6.61	0.24
149	2,2′,3,4′,5′,6-Hexachlorobiphenyl	0.107	−0.022	6	6.41	6.42	−0.01
151	2,2′,3,5,5′,6-Hexachlorobiphenyl	0.111	−0.027	6	6.42	6.62	−0.20
153	2,2′,4,4′,5,5′-Hexachlorobiphenyl	0.110	−0.025	6	6.80	6.61	0.19
154	2,2′,4,4′,5,6′-Hexachlorobiphenyl	0.108	−0.024	6	6.65	6.43	0.22
155	2,2′,4,4′,6,6′-Hexachlorobiphenyl	0.108	−0.021	6	6.54	6.60	−0.06
156	2,3,3′,4,4′,5-Hexachlorobiphenyl	0.119	−0.036	6	7.44	7.06	0.38
158	2,3,3′,4,4′,6-Hexachlorobiphenyl	0.115	−0.030	6	6.78	6.93	−0.15
163	2,3,3′,4′,5,6-Hexachlorobiphenyl	0.115	−0.030	6	6.78	6.93	−0.15
164	2,3,3′,4′,5′,6-Hexachlorobiphenyl	0.110	−0.024	6	6.63	6.67	−0.04
165	2,3,3′,5,5′,6-Hexachlorobiphenyl	0.115	−0.030	6	7.00	6.93	0.07
167	2,3′,4,4′,5,5′-Hexachlorobiphenyl	0.112	−0.027	6	7.29	6.74	0.55
169	3,3′,4,4′,5,5′-Hexachlorobiphenyl	0.112	−0.025	6	7.55	6.85	0.70
170	2,2′,3,3′,4,4′,5-Heptachlorobiphenyl	0.116	−0.03	7	7.08	7.16	−0.08
172	2,2′,3,3′,4,5,5′-Heptachlorobiphenyl	0.116	−0.031	7	7.21	7.11	0.10
174	2,2′,3,3′,4,5,6′-Heptachlorobiphenyl	0.113	−0.028	7	6.85	6.92	−0.07
175	2,2′,3,3′,4,5′,6-Heptachlorobiphenyl	0.115	−0.031	7	6.92	6.99	−0.07
176	2,2′,3,3′,4,6,6′-Heptachlorobiphenyl	0.112	−0.028	7	6.55	6.80	−0.25
177	2,2′,3,3′,4,5′,6′-Heptachlorobiphenyl	0.114	−0.030	7	6.73	6.92	−0.19
178	2,2′,3,3′,5,5′,6-Heptachlorobiphenyl	0.114	−0.030	7	6.85	6.92	−0.07
179	2,2′,3,3′,5,6,6′-Heptachlorobiphenyl	0.111	−0.027	7	6.41	6.73	−0.32
180	2,2′,3,4,4′,5,5′-Heptachlorobiphenyl	0.115	−0.031	7	7.21	6.99	0.22
181	2,2′,3,4,4′,5,6-Heptachlorobiphenyl	0.119	−0.034	7	7.13	7.30	−0.17
182	2,2′,3,4,4′,5,6′-Heptachlorobiphenyl	0.113	−0.028	7	6.92	6.92	0.00
183	2,2′,3,4,4′,5′,6-Heptachlorobiphenyl	0.115	−0.031	7	7.04	6.99	0.05
185	2,2′,3,4,5,5′,6-Heptachlorobiphenyl	0.118	−0.034	7	6.99	7.17	−0.18
188	2,2′,3,4′,5,6,6′-Heptachlorobiphenyl	0.111	−0.027	7	6.78	6.73	0.05
189	2,3,3′,4,4′,5,5′-Heptachlorobiphenyl	0.119	−0.033	7	7.72	7.35	0.37
190	2,3,3′,4,4′,5,6-Heptachlorobiphenyl	0.121	−0.036	7	7.08	7.42	−0.34
191	2,3,3′,4,4′,5′,6-Heptachlorobiphenyl	0.119	−0.033	7	7.21	7.35	−0.14
192	2,3,3′,4,5,5′,6-Heptachlorobiphenyl	0.122	−0.036	7	7.21	7.54	−0.33
193	2,3,3′,4′,5,5′,6-Heptachlorobiphenyl	0.118	−0.033	7	7.21	7.23	−0.02
194	2,2′,3,3′,4,4′,5,5′-Octachlorobiphenyl	0.119	−0.033	8	7.62	7.47	0.15
195	2,2′,3,3′,4,4′,5,6-Octachlorobiphenyl	0.121	−0.036	8	7.35	7.54	−0.19
196	2,2′,3,3′,4,4′,5,6′-Octachlorobiphenyl	0.118	−0.033	8	7.43	7.35	0.08

(*continued on next page*)

Table 4 (*continued*)

IUPAC No.	Compounds	Descriptors			$\log K_{ow}$[a] values		
		ω	E_{LUMO}	N_{Cl}	Exp.[b]	Calculated	Residual[c]
203	2,2′,3,4,4′,5,5′,6-Octachlorobiphenyl	0.121	−0.036	8	7.49	7.54	−0.05
204	2,2′,3,4,4′,5,6,6′-Octachlorobiphenyl	0.119	−0.034	8	7.48	7.41	0.07
205	2,3,3′,4,4′,5,5′,6-Octachlorobiphenyl	0.125	−0.039	8	7.62	7.85	−0.23
206	2,2′,3,3′,4,4′,5,5′,6-nonachlorobiphenyl	0.124	−0.039	9	7.94	7.84	0.10
207	2,2′,3,3′,4,4′,5,6,6′-nonachlorobiphenyl	0.122	−0.036	9	7.88	7.77	0.11

[a] With ω (in au), E_{LUMO} (in au) and N_{Cl} as descriptors.
[b] Experimental data as obtained from Refs. 12 and 41.
[c] The residual is the difference between experimental and predicted $\log K_{ow}$ values.

($r^2 = 0.914$) and cross-validated squared correlation coefficient ($r^2_{cv} = 0.909$) value indicating the significance of the developed model.

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